

# Residues of Veterinary Medicinal Products (antibiotics) in shrimp exported from India to the European Union (EU)

## Trends in the last decade

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*Focal Points at a Glance: The authors give an account of the RASFF (Rapid Alert System for Food and Feed) followed by the E.U and the number of cases in which antibiotics have been found in shrimp shipments, originating from India for the period January 2003 to November 2014. An informative account.*

### Abstract

The Rapid Alert System for Food and Feed (RASFF) notifications pertaining to shrimp exported from India to the European Union (EU) during the period 01 Jan, 2003 to 01 Nov, 2014 was analysed and the trends are presented, antibiotic residue wise, shrimp species-wise, notifying country wise. A total of 228 RASFF notifications were notified of which 76% were because of the presence of antibiotic residues. The notifications showed an increasing trend from 2003, peaked in 2008 and 2009 followed by a decreasing trend. However, in 2014 there was a spurt in RASFF notifications due to antibiotic residues. The period between 2005 and 2009, was a turbulent period with two-thirds of the total notifications due to presence of antibiotic residues; of which 35% of the complaints were recorded in 2008 and 2009. Two thirds of notifications were notified by United Kingdom (36%) and Belgium (33%). Nitrofurans (metabolite) furazolidone (AOZ) (44%), nitrofurazone (SEM) (37%), were the major causes of notifications, followed by Chloramphenicol (6%) and Oxytetracycline (2%). Of the total RASFF notifications due to antibiotic residues, 39% were from black tiger, 31% from scampi and 6% from vannamei. 94% of the complaints involving scampi were due to SEM, 85% of the complaints involving black tiger were due to AOZ and 90% of the notifications involving vannamei were due to AOZ. The reported level of SEM in shrimp ranged between

1.1 and 170ppb and AOZ ranged from 1.1 to 150 ppb. The data shows that the trend in vannamei complaints might progress similar to that of black tiger. All the stakeholders of shrimp production, processing, distribution, promotion and regulation should take appropriate measures to mitigate the menace of residues of veterinary medicinal products (antibiotic residues) in shrimp exported from India. Steps to minimise the incidence of antibiotic residues in shrimp exports are suggested.

### Introduction

Worldwide, between 2000 and 2010, consumption of antibiotic drugs increased by 36% (from 54, 083, 964, 813 standard units to 73, 620, 748, 816 standard units) and India was the single largest consumer of antibiotics in the world in 2010, followed by China and the United States (Van Boeckel *et al.*, 2014). Increase in antibiotic drug consumption is the major contributor for development of antibiotic resistance in pathogenic bacteria. This issue has to be addressed by the medical fraternity but there is another issue of antibiotics i.e. *the problem of veterinary medicinal drugs* in shrimp is plaguing the Indian shrimp export. Indian marine product exports witnessed impressive growth from 37,175 tonnes in 1970 to 9,83,756 tonnes in 2013-14. In terms of value, the increase was from US \$ 47.38 million (Rs. 35.54 crores) in 1970 to US \$ 5007.70 million (Rs. 30,213.26 crores) in 2013-14. Frozen shrimp continued to be

the major export value item accounting for a share of 64.12% of the total US\$ earnings of which the contribution of cultured shrimp was 73.31% (source: <http://www.mpeda.com>).

Residues of veterinary medicinal products in food are potentially harmful to the consumers eg., chloramphenicol causes aplastic anaemia and nitrofurans are carcinogenic. The EU has established a minimum required performance limit (MRPL) of 1 µg/kg (1 ppb) for nitrofurans metabolites and 0.3 µg/kg for chloramphenicol in aquaculture products (EU, 2003). However, EU has 'zero tolerance' to nitrofurans which means 'any confirmed concentration of any of the metabolites is a non-compliance'. It is pertinent to note that nitrofurans (furazolidone, furaltadone, nitrofurazone, nitrofurantoin, furylfuramide, nifuratel, nifuroxime, nifurprazine) and chloramphenicol etc., are banned for use in aquaculture in India. During 2014 (up to the end of Oct), Indian shrimp exports to the European Union (EU) witnessed eleven rejections due to the presence of antibiotics residue AOZ in shrimp, mainly *Litopenaeus vannamei* exported from India. In this context, an analysis of the RASFF complaints pertaining to shrimp exported from India during the period 2003 to 2013 and notifications up to Oct, 2014 was carried out to understand the trend in the antibiotic complaints.

*The Rapid Alert System for Food and Feed (RASFF) of the EU is a key tool that is*



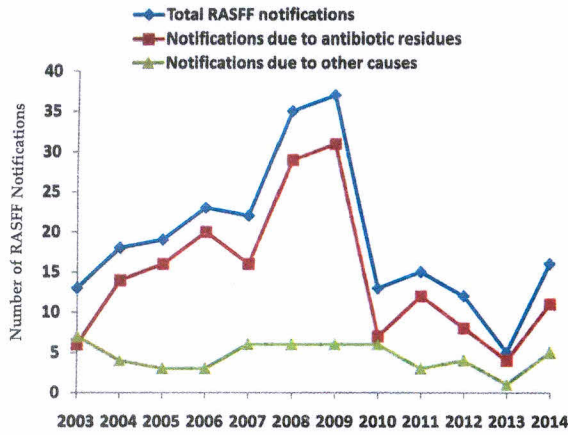


Fig 1. RASFF notifications of shrimp exported from India to the European Union

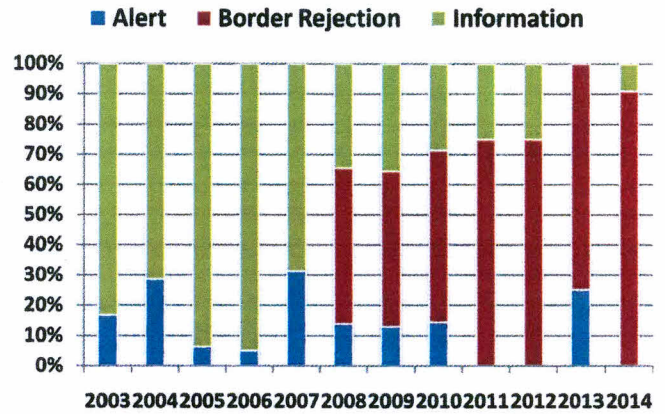


Fig 2. Categories of RASFF notifications pertaining to antibiotic residues

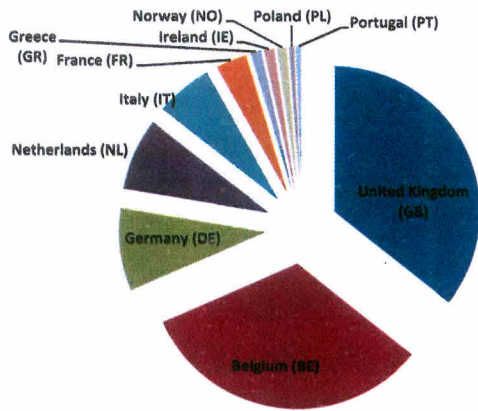


Fig3. Notifying country-wise trend of RASFF complaints due to antibiotic residues in shrimp exported from India.

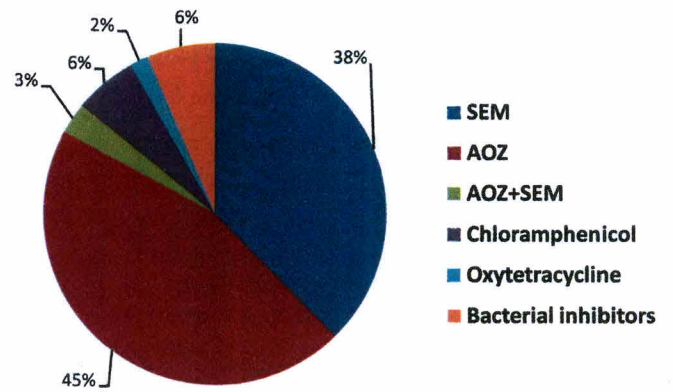


Fig 4. Trend in the RASFF notifications antibiotic wise

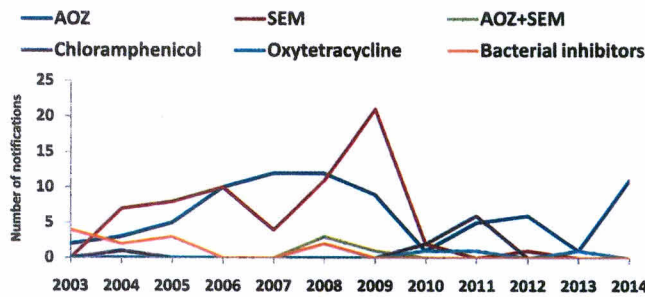


Fig 5. The trend in the RASFF complaints (antibiotic residue-wise) of shrimp exported from India (SEM = semicarbazide; AOZ = 3-amino-2-oxazolidinone)

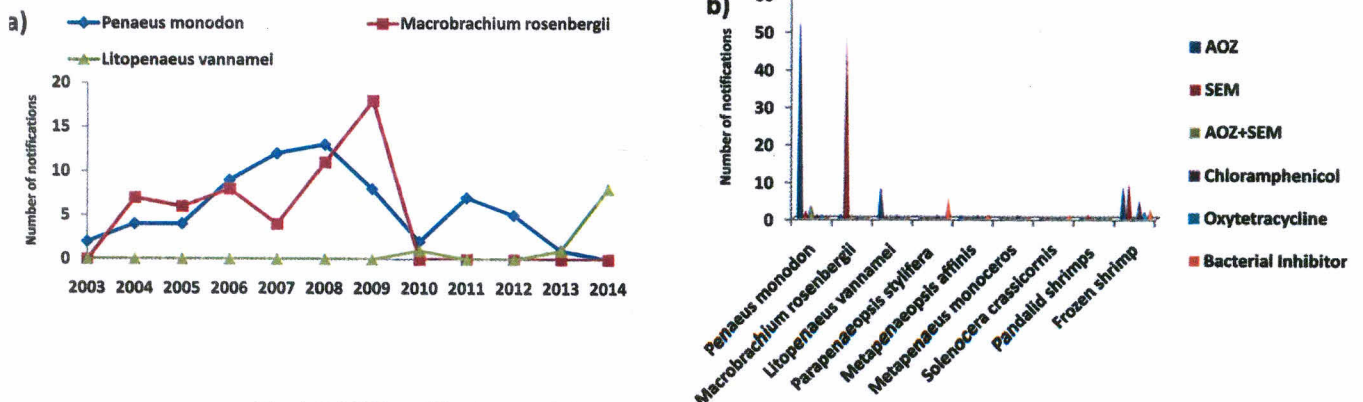


Fig 6. RASFF notifications - Shrimp species wise trend during the period 2003 to 2014



used to avert food safety risks in food and feed before they can harm consumers. Four types of notifications viz., alert notifications, information notifications, border rejection and news are reported by the European Commission. *Alert notifications* are sent when food or feed presenting a serious risk is available in the market and when rapid action is required. *Information notifications* are used in the same situation, but when the other members do not have to take rapid action because the product is not on the market or the risk is not considered to be serious. *Border rejections* concern food and feed consignments that have been tested and rejected at the external borders of the EU when a health risk has been detected. Border rejections are transmitted to all 28 EU Member States, Iceland, Liechtenstein, Norway and Switzerland to ensure that the rejected product does not re-enter the EU through another border post. Lastly, any information related to the safety of food and feed products which has not been communicated as an alert or an information notification, but which is judged valuable for the control authorities, is transmitted to the members under the heading *News*. The RASFF notifications shown in the RASFF portal represent a new case reported on a health risk detected in one or more consignments of a food or feed.

The RASFF notifications related to residues of veterinary medicinal products in shrimp exported from India were accessed from the RASFF portal (<https://webgate.ec.europa.eu/rasff-window/portal/event>). The RASFF notifications that included alerts, border rejections and notifications pertaining to shrimp exported from India to the EU during the period 01 Jan, 2003 to 01 Nov 2014, was analysed and grouped antibiotic residue wise, shrimp species wise, notifying country wise

**1. Trend of total RASFF notifications of shrimp exported from India to the European Union:**

During this period a total of 228 RASFF notifications (Table 1) were notified, of which 76% were due to the presence of antibiotic residues. The RASFF notifications showed an increasing trend from 2003, peaked in 2008 and 2009 followed by a decreasing trend (Fig 1). However, in 2014 there was a spurt in RASFF notifications due to antibiotic residues. It is pertinent to note that the complaints due to antibiotic residues dictated the trend of total RASFF notifications. The period between 2005 and

2009 was a turbulent period with two-thirds of the total RASFF notifications due to presence of antibiotic residues; of which 35% of the complaints were recorded in 2008 and 2009. The RASFF notifications up to 2007 were predominantly information notifications but after 2008 the border rejections notifications dominated the total RASFF notifications (Fig 2).

**2. Notifying country-wise trend of RASFF complaints:**

Two thirds of RASFF notifications due to the presence of antibiotic residues were notified by United Kingdom (36%) and Belgium (33%). Other countries that delivered notifications were Germany (9%), Netherlands (8%), Italy (6%), France (3.5%), Greece (1%), Ireland (1%), Norway (1%), Poland (1%) and Portugal (1%) (Fig 3). Antibiotic residue wise, 48% and 36% of the SEM complaints were reported by Belgium & United Kingdom and 44% and 25% of AOZ complaints were reported by United Kingdom & Belgium. 66% of oxytetracycline complaints were reported by United Kingdom and 40% of chloramphenicol complaints were reported by Belgium.

**3. Antibiotic residue-wise trend of RASFF complaints**

The antibiotic residues which were notified were nitrofurantoin (metabolite) nitrofurazone (SEM; semicarbazide), nitrofurantoin (metabolite) furazolidone

(AOZ; 3-amino-2-oxazolidinone presence of both AOZ & SEM chloramphenicol, oxytetracycline or bacterial inhibitors (Fig 4). SEM and AOZ were responsible for 86% of the RASFF complaints. AOZ (44%), SEM (37%), were the major cause followed by Chloramphenicol (6%) and Oxytetracycline (2%). 3% of the notifications were due to the presence of both AOZ and SEM in the same consignment. 6% of the notifications were categorised as bacterial inhibitors and these were mainly reported prior to 200

The trend in the RASFF notification antibiotic wise is depicted in Fig 1. Maximum SEM complaints were reported in 2009 and maximum AOZ notification were reported in 2007 and 2008. The number of SEM notifications drastically decreased after 2010 onwards which may mostly be attributed to the opinion that SEM may be present due to environmental contamination and therefore not to be considered as sufficient proof for illegal use of veterinary medicines (RASFF, 2013) and also due to the drastic reduction in scampi exports from India. SEM notification were mainly reported in scampi. The decrease in AOZ notifications from 2010 onwards may be attributed to the concerted precautionary efforts of the regulatory agencies, research institutes, shrimp processors and farmers. Measures such as pre-harvest testing c

**Table: RASFF notifications of shrimp exported from India to the European Union during the period 01 Jan, 2003 to 01 Nov, 2014**

Year	Total RASFF notifications	Notifications due to antibiotic residues	Notifications due to other causes
2003	13	6	7
2004	18	14	4
2005	19	16	3
2006	23	20	3
2007	22	16	6
2008	35	29	6
2009	37	31	6
2010	13	7	6
2011	15	12	3
2012	12	8	4
2013	5	4	1
2014	16	11	5
<b>Total</b>	<b>228</b>	<b>174</b>	<b>54</b>

shrimps, establishing traceability, awareness campaigns, seminars, farm audits etc. sensitised the stake holders regarding the problem of antibiotic residues. RASFF notifications pertaining to chloramphenicol and oxytetracycline were reported frequently from 2010 onwards.

**4. Shrimp species-wise trend of RASFF notifications:**

RASFF notifications due to antibiotics were reported in *Penaeus monodon* (black tiger), *Macrobrachium rosenbergii* (scampi, giant freshwater prawn), *Litopenaeus vannamei* (vannamei shrimp, white leg shrimp), *Parapenaeopsis stylifera*, *Metapenaeopsis affinis*, *Metapenaeus monoceros*, *Solenocera crassicornis*, *Pandalid shrimp* and in some cases the species simply mentioned as frozen shrimp. Of the total RASFF notifications due to antibiotic residues, 39% were from black tiger, 31% from scampi and 6% from vannamei and their trend during the period 2003 to 2014 is given in Fig 6a. Notifications in scampi reached a peak in 2009 and black tiger in 2008. Vannamei notifications first appeared in 2010 and reached a maximum in 2014. 94% of the complaints involving scampi were due to SEM, 85% of the complaints involving black tiger were due to AOZ and 90% of the RASFF notifications involving vannamei were due to AOZ (Fig 6b). There was wide variation in the quantity of antibiotic residue reported from shrimp exported from India. The level of SEM in shrimp ranged between 1.1 and 170ppb with a mean value of 8.27±19.6 and AOZ ranged from 1.1 to 150 ppb with a mean value of 14.1±25.3.

**5. Nitrofurans and their metabolites**

Nitrofurans are a group of synthetic antibiotics that were chemically derived from furans and contain a characteristic 5-nitrofuranyl ring. Nitrofurans include nitro-furazone, nitrofurantoin, furaltadone and furazolidone. Nitrofuranyl antibiotics were banned from use in the EU due to concerns of carcinogenicity of the drug residues and their potential harmful effects on human health and therefore food imported into the EU should be free of nitrofurans. Nitrofurans were previously used as growth promoters and prophylactic agents because they are cheap and effective. Furazolidone has a broad antimicrobial spectrum and is active against both gram-positive and gram-negative bacteria and has been used in human and veterinary medicine to treat intestinal infections. Nitrofurans parent compounds

metabolise rapidly after ingestion by the shrimp to form corresponding tissue bound metabolites (nitrofurazone metabolizes to semicarbazide-SEM, nitrofurantoin to 1-aminohydantoin-AHD, furaltadone to 3-amino-5-morpholinomethyl-1,3-oxazolidinone-AMAZ and furazolidone metabolises to 3-amino-2-oxazolidinone-AOZ). The nitrofuranyl parent compounds have a short *in vivo* half life of 7 to 63 minutes result in the depletion of nitrofurans in blood and tissue but the nitrofuranyl metabolites (SEM, AHD, AMAZ and AOZ) bind to tissue proteins in the body for many weeks after treatment (Vass *et al.*, 2008). Nitrofuranyl metabolites are stable during storage and are not destroyed by cooking, frying, grilling, roasting and microwaving of meat. Owing to these attributes, nitrofuranyl metabolites are the preferred compounds for monitoring compliance. The EU has established a MRPL of 1 µg/kg for nitrofuranyl metabolites in aquaculture products (EU, 2003). Nitrofuranyl (metabolites) mainly AOZ and SEM either present singly or combined were the prime cause of RASFF notifications involving shrimp exported from India during 2003 to 2014. RASFF notifications were due to nitrofuranyl (metabolites) in 100%, 97% and 90% of *M. rosenbergii*, *P. monodon* (black tiger shrimp) and *L. vannamei*, respectively.

The year 2014 witnessed an increase in the RASFF notifications due to the presence of antibiotic residues mainly nitrofuranyl (metabolite) Furazolidone (AOZ) in *L. vannamei* shrimp exported from India. Till that time, the RASFF notifications were in a decreasing trend that started in 2009. The quantity of shrimp exported from India increased significantly during the last four years. The quantity of frozen shrimp exported by India in 2010-11, 2011-12, 2012-13 and 2013-14 was 1,51,465 t, 1,89,125, 2,28,620 and 3,01,435, respectively. The frozen shrimp export in 2014-15 may follow similar trend. Keeping this in view, it may be argued that the number of rejections due to antibiotic residues *vis-à-vis* the quantity of shrimp exported may not be high. The data show that the trend in vannamei complaints might progress similar to that of black tiger as 90% of the rejections in vannamei were due to the presence of AOZ.

The issue of increase in the RASFF notifications due to nitrofuranyl (metabolite) furazolidone (AOZ) in *L. vannamei* shrimp has to be addressed on priority basis or else the situation will reach the same or even worse proportion than that was seen during the turbulent

periods of 2005-2009. Apart from this, recently high level of chloramphenicol was detected in enzyme preparations (xylanase, amylase, pectinase, glucanase and cellulose enzyme) that are used in food and feed (RASFF, 2014), which might be a future concern. Considering these issues, all the stakeholders of shrimp production, processing, distribution, promotion and regulation should take appropriate measures to mitigate the menace of residues of veterinary medicinal products (antibiotic residues) in shrimp exported from India.

**Steps to minimise the incidence of antibiotic residues in shrimp exports:**

**For Shrimp Hatcheries:-**

- i) Banned antibiotics should not be used.
- ii) It should be ensured that Feed and feed supplements, medicines used in hatcheries are free from banned antibiotics.
- iii) Better water management practices should be adopted.
- iv) Records should be kept for all inputs.

**For Aquaculture farms:**

- i) All farms to be registered with designated authorities.
- ii) Unlabeled drugs and banned antibiotics should not be used.
- iii) Scientific farming practices should be used with appropriate stocking densities and water management.
- iv) Feed and feed supplements, medicines used in farming should be free from banned antibiotics.
- v) Periodic monitoring of the inlet water source (canals) should be done to check the presence of banned antibiotics and chemicals.
- vi) The water and soil of shrimp farms that were recently converted from fish farms have to be tested for banned antibiotics
- vii) Records should be kept for all inputs.

**Feed and other inputs (probiotics, chemicals) suppliers:-**

- i) Products supplied for shrimp aquaculture should be tested and labeled as free from banned antibiotics.
- ii) It must be ensured that ingredients used for manufacturing are free from banned antibiotics.

**Shrimp processing establishments**

- i) Pre-harvest tested shrimp only may

be accepted and processed.

- ii) Infrastructure for in-house testing for antibiotic residues may be established and adequate training to the personnel may be provided.
- iii) Effective traceability should be ensured.
- iv) All additives should be tested for banned antibiotics.
- v) Periodic farm audits may be conducted.
- vi) The farmers and suppliers may be sensitised on non-usage banned of antibiotics.

**Laboratories approved by competent authority for testing antibiotic residues.**

- i) Strict sampling procedure should be adhered to. There needs to be participation in inter laboratory proficiency testing with analytical and research laboratories in India and abroad.

**Research institutes**

- i) Natural, organic and GRAS alternatives for antibiotics to control disease in farms and hatcheries may be developed.
- ii) Natural antimicrobials, organic acids, essential oils bacteriocins, bacteriophages, probiotics, etc may be considered as potential alternatives for research.
- iii) Compounds advocated should provide protection from shrimp pathogens but should not adversely affect the survivability of post-larvae and shrimps.

**Government agencies:**

- i) Testing of inputs used in shrimp hatcheries and shrimp aquaculture farms such as feed, probiotics, feed supplements and chemicals to made mandatory.
- ii) Antibiotics to be labeled as not for use in shrimp aquaculture.
- iii) Residue monitoring under National Residue Control Plan (NRCP) to increase surveillance in shrimp farming areas which were traced as per RASFF notifications.
- iv) Training programmes may be organised at regular intervals for quality control personnel in processing establishments on different methods of assessing

antibiotic residues and chemical contaminants.

- v) Awareness campaigns on non-usage of antibiotics in the shrimp culture system may be conducted.
- vi) A regulatory/statutory body to approve the personnel involved in shrimp disease diagnosis and prescribing drugs for aquaculture may be created.

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